Mr. MERRILL. Mr. Gordon, Dr. Crout makes a point that is too important not to reemphasize. And we have been spending a lot of time in the Food and Drug Administration trying to insist that drug manufacturers back up their claims with adequate and well-controlled clinical studies—scientific evidence and not on opinion. And for the very same reason we are reluctant to rely upon our own instinctive judgments. We would like the backing of the scientific community, and strong scientific evidence. We think it is obtainable. But we want to be sure.

The CHAIRMAN. Go ahead Doctor.

Dr. SCHMIDT. At hearings before this subcommittee this past January, Dr. P. J. Palumbo reported that a retrospective study of diabetic patients treated at the Mayo Clinic suggests that survival was lower in those patients treated with hypoglycemic agents compared to those patients treated with either insulin or diet. Dr. Palumbo's full study has not yet been published.[1]

Another study, a retrospective study of patients treated at the Joslin Clinic reported in a doctoral thesis by P. Kanarek, can be interpreted as providing results that are consistent with those of the UGDP. Although we have seen this study, it has not yet been subjected to a full review by statistical and epidemiological experts.[2]

At this point we can say that certain subgroups of insulin-treated patients appear to have better survival rates than tolbutamide-treated patients with comparable glucose abnormalities. Studies of this type, however, always present problems in interpretation because of doubts regarding comparability of treatment groups and because treatments are not randomly allocated. Thus, although the retrospective studies of Palumbo and Kanarek may or may not, when fully analyzed, add support to the UGDP findings, the prospective UGDP study must be accorded far greater weight and is alone a sufficient basis for our proposed actions.

Doctors Tan, Bradley, Gleason and Soeldner have reported on the long-term effects—4 years—of hypoglycemic agents on the oral glucose tolerance test and blood lipids in chemical diabetics at the annual meeting of the American Diabetes Association, in 1973—abstract in "Diabetes" 22 (suppl. 1): 290, 1973. The investigators' abstract reported there was no significant difference in the improvement in glucose tolerance between patients receiving oral hypoglycemic agents and patients receiving a placebo. The full report of this study has not yet been published, but it appears that the investigators studied glucose tolerance on the day following discontinuation of the drugs. Their findings thus would indicate only that the oral agents do not lead to improved glucose tolerance in the absence of continued use of the drug.

In another study, Dr. R. W. Wissler, in an FDA-supported investigation, examined the chronic effects of tolbutamide in the rhesus monkey. He found that coronary artery lesions were almost two times more ferquent and three times more severe in the tolbutamide-treated animals than in the control animals. FDA recently received

[1] Hearings before the Subcommittee on Monopoly, Select Committee on Small Business, U.S. Senate, 94th Congress, 1st Session, on Safety, Efficacy, and Use of Antibiotics—Clindamycin and Lincomycin, January 28, 29, and July 8, 1975, Part 27.

[2] See study by P. Kanarek, page 13393.